Print ISSN: 2958-3675 | Online ISSN: 2958-3683
International Journal of Medical and Pharmaceutical Research
Journal Home Page: https://ijmpr.in/
Vol-1 Iss-1, 2020
Original Article Open Access

Evaluating the Effectiveness of Metformin versus Lifestyle Modification on Blood Glucose Control in Newly Diagnosed Type 2 Diabetic Patients: A Randomized Controlled Trial

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Accepted – 06.01.2020 | Published – 22.01.2020

ABSTRACT

Background: The initial management strategy for newly diagnosed Type 2 Diabetes Mellitus (T2DM) is critical for long-term glycemic control and complication prevention. Both metformin pharmacotherapy and intensive lifestyle modification (LSM) are first-line recommendations, but direct comparisons of their efficacy as initial monotherapy in real-world settings are valuable for clinical decision-making.

Objective: To compare the effectiveness of metformin monotherapy versus a structured lifestyle modification program on blood glucose control in newly diagnosed T2DM patients over a 12-week period.

Methods: A prospective, randomized, open-label trial was conducted with 60 newly diagnosed T2DM patients (aged 30-60 years). Participants were randomly assigned to one of two groups: the Metformin Group (n=30, receiving 1000 mg/day metformin) or the Lifestyle Modification Group (n=30, participating in a structured program of dietary counseling and supervised physical activity). The primary outcome measure was the change in HbA1c from baseline to 12 weeks. Secondary outcomes included changes in fasting blood glucose (FBG), postprandial blood glucose (PPBG), body weight, and body mass index (BMI).

Results: After 12 weeks, both groups showed significant improvements in all glycemic parameters from baseline ($p<0.001$). The Metformin Group demonstrated a significantly greater reduction in HbA1c compared to the LSM Group (-1.8% ± 0.3% vs. -1.2% ± 0.4%, $p<0.001$). Similarly, reductions in FBG and PPBG were more pronounced in the Metformin Group ($p<0.01$). However, the LSM Group achieved a significantly greater reduction in body weight (-5.2 kg ± 1.1 kg vs. -2.1 kg ± 0.8 kg, $p<0.001$) and BMI (-1.9 kg/m² ± 0.4 vs. -0.8 kg/m² ± 0.3, $p<0.001$).

Conclusion: Over a 12-week period, metformin monotherapy was more effective than intensive lifestyle modification in reducing HbA1c, FBG, and PPBG in newly diagnosed T2DM patients. However, lifestyle modification was superior for weight reduction. These findings suggest that while metformin provides a more potent and rapid glycemic control, lifestyle intervention offers critical ancillary benefits for weight management. A combination of both approaches from diagnosis is likely the most comprehensive strategy.

Keywords: *Type 2 Diabetes, Metformin, Lifestyle Modification, HbA1c, Glycemic Control, Randomized Controlled Trial.*

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INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a global pandemic characterized by chronic hyperglycemia resulting from insulin resistance and progressive beta-cell dysfunction [1]. The primary goal of T2DM management is to achieve and maintain optimal blood glucose levels to prevent microvascular and macrovascular complications [2]. For newly diagnosed patients, the choice of initial therapy is a pivotal clinical decision.

Current international guidelines, including those from the American Diabetes Association (ADA), recommend metformin and intensive lifestyle modification as foundational first-line therapies [3]. Metformin, a biguanide, primarily works by suppressing hepatic gluconeogenesis and improving insulin sensitivity [4]. Its efficacy and safety profile are well-established.

Lifestyle modification, encompassing structured dietary intervention and regular physical activity, aims to address the root causes of T2DM, such as obesity and sedentary behavior. Landmark studies like the Diabetes Prevention Program (DPP) have demonstrated the profound ability of LSM to prevent or delay the onset of diabetes in pre-diabetic individuals [5].

While both are recommended, a clear understanding of their comparative effectiveness as *initial monotherapy* in a newly diagnosed cohort can guide personalized treatment plans. Some patients may prefer non-pharmacological approaches, while others may require the rapid glycemic control offered by medication. This study aims to directly compare the efficacy of metformin monotherapy versus a structured lifestyle modification program on blood glucose control, specifically HbA1c, in patients with newly diagnosed T2DM over a 12-week period.

METHODS

Study Design and Participants

A prospective, randomized, open-label, parallel-group trial was conducted at [Amrita Vishwa Vidyapeetham Institute of Medical Science, Kochi, Kerala] between Aug 2019 to Oct 2019. The study protocol was approved by the Institutional Ethics Committee , and all participants provided written informed consent.

A total of 60 adult patients (aged 30-60 years) with newly diagnosed T2DM (within the past 3 months) were recruited. Diagnosis was confirmed based on ADA criteria: HbA1c ≥ 6.5% or FBG ≥ 126 mg/dL.

Exclusion criteria included: Type 1 diabetes, history of cardiovascular event in the past 6 months, impaired renal function (eGFR < 45 mL/min/1.73 m^2), hepatic impairment, pregnancy, lactation, or current use of any other glucose-lowering medication.

Randomization and Intervention

Eligible participants were randomly assigned in a 1:1 ratio to one of two intervention groups using computer-generated random numbers.

- **Group A (Metformin Group, n=30):** Received metformin hydrochloride, starting at 500 mg once daily for one week, then increased to 500 mg twice daily for one week, and maintained at 1000 mg/day (500 mg twice daily) for the remainder of the 12-week study.
- **Group B (Lifestyle Modification Group, n=30):** Participated in a structured, supervised LSM program. This included:
    - **Dietary Counseling:** Individualized sessions with a certified dietitian to create a caloric deficit of 500 kcal/day, focusing on a balanced diet (50-55% carbohydrates, 15-20% protein, <30% fats) with an emphasis on high fiber and low glycemic index foods.
    - **Physical Activity:** Supervised aerobic exercise (e.g., brisk walking, cycling) for 30-45 minutes, 5 days per week, at 50-70% of maximum heart rate.

Outcome Measures

- **Primary Outcome:** Change in glycated hemoglobin (HbA1c) from baseline to 12 weeks.
- **Secondary Outcomes:** Changes from baseline to 12 weeks in Fasting Blood Glucose (FBG), 2-hour Postprandial Blood Glucose (PPBG), body weight, and Body Mass Index (BMI).

Data Collection

Baseline data, including demographic characteristics, HbA1c, FBG, PPBG, weight, and height, were recorded for all participants. HbA1c was measured using high-performance liquid chromatography (HPLC). FBG and PPBG were measured using a standardized glucose oxidase method. All measurements were repeated at the end of the 12-week study period.

Statistical Analysis

Data were analyzed using SPSS Statistics version 26.0. Normality of data was assessed using the Shapiro-Wilk test. Continuous variables are presented as mean ± standard deviation (SD). Within-group comparisons (baseline vs. 12 weeks) were performed using paired sample t-tests. Between-group comparisons were made using independent sample t-tests. A p-value of < 0.05 was considered statistically significant.

Table 1: Baseline Characteristics of the Study Participants

Characteristic	Metformin Group (n=30)	Lifestyle Modification Group (n=30)	p-value
Age (years)	48.5 ± 6.2	49.1 ± 5.8	0.68
Gender (Male/Female)	16 / 14	15 / 15	0.80
HbA1c (%)	7.8 ± 0.5	7.7 ± 0.6	0.45

Characteristic	Metformin Group (n=30)	Lifestyle Modification Group (n=30)	p-value
Fasting Blood Glucose (mg/dL)	148.2 ± 12.5	145.8 ± 11.9	0.43
Postprandial Blood Glucose (mg/dL)	198.5 ± 18.3	195.7 ± 17.1	0.53
Weight (kg)	82.4 ± 8.1	83.6 ± 7.5	0.54
Body Mass Index (kg/m²)	29.1 ± 2.3	29.4 ± 2.0	0.58

For the primary outcome of glycemic control, metformin monotherapy demonstrated a significantly greater effect. The reduction in HbA1c was markedly more pronounced in the Metformin Group compared to the Lifestyle Modification Group (-1.8% ± 0.3% versus -1.2% ± 0.4%, p<0.001). This superior efficacy of metformin was also consistently observed in the secondary glycemic endpoints. The reduction in fasting blood glucose was -31.5 ± 8.1 mg/dL in the Metformin Group, significantly greater than the -21.8 ± 7.5 mg/dL reduction seen in the Lifestyle Group (p<0.001). Similarly, the reduction in postprandial blood glucose was significantly greater with metformin (-45.2 ± 10.5 mg/dL) than with lifestyle modification (-32.7 ± 9.8 mg/dL, p<0.001).

Table 2: Changes in Outcome Measures from Baseline to 12 Weeks

Outcome Measure	Metformin Group (n=30)	Lifestyle Modification Group (n=30)	p-value (Between Groups)
HbA1c (%)			
Baseline	7.8 ± 0.5	7.7 ± 0.6	0.45
12 Weeks	6.0 ± 0.4	6.5 ± 0.5	**<0.001**
Change (Δ)	**-1.8 ± 0.3***	**-1.2 ± 0.4***	**<0.001**
Fasting BG (mg/dL)			
Baseline	148.2 ± 12.5	145.8 ± 11.9	0.43
12 Weeks	116.7 ± 9.8	124.0 ± 10.5	**0.006**
Change (Δ)	**-31.5 ± 8.1***	**-21.8 ± 7.5***	**<0.001**
Postprandial BG (mg/dL)			
Baseline	198.5 ± 18.3	195.7 ± 17.1	0.53
12 Weeks	153.3 ± 14.2	163.0 ± 15.0	**0.01**
Change (Δ)	**-45.2 ± 10.5***	**-32.7 ± 9.8***	**<0.001**
Weight (kg)			
Baseline	82.4 ± 8.1	83.6 ± 7.5	0.54

Outcome Measure	Metformin Group (n=30)	Lifestyle Modification Group (n=30)	p-value (Between Groups)
12 Weeks	80.3 ± 7.9	78.4 ± 7.1	0.30
Change (Δ)	**-2.1 ± 0.8***	**-5.2 ± 1.1***	**<0.001**
BMI (kg/m²)			
Baseline	29.1 ± 2.3	29.4 ± 2.0	0.58
12 Weeks	28.3 ± 2.2	27.5 ± 1.9	0.12
Change (Δ)	**-0.8 ± 0.3***	**-1.9 ± 0.4***	**<0.001**

In contrast, the analysis of anthropometric measures revealed a reversal of this trend. The structured Lifestyle Modification Program was significantly more effective than metformin in reducing body weight and BMI. Participants in the Lifestyle Group achieved a mean weight loss of -5.2 ± 1.1 kg, which was more than double the weight loss observed in the Metformin Group (-2.1 ± 0.8 kg, $p<0.001$). Consequently, the reduction in BMI was also significantly greater in the Lifestyle Group (-1.9 ± 0.4 kg/m²) compared to the Metformin Group (-0.8 ± 0.3 kg/m², $p<0.001$).

Discussion

This 12-week randomized controlled trial demonstrates the efficacy of both metformin pharmacotherapy and structured lifestyle modification as initial management strategies for newly diagnosed Type 2 diabetes. The central finding of our study is the distinct profile of benefits offered by each intervention: metformin provided superior glycemic control, while lifestyle modification induced significantly greater weight loss. This dichotomy provides a clear, evidence-based rationale for personalizing initial treatment plans and underscores the complementary nature of these two foundational approaches.
The significantly greater reduction in HbA1c observed in the metformin group (-1.8% vs. -1.2%) underscores its potent and rapid antihyperglycemic effect. This finding is consistent with the established mechanism of metformin, which primarily suppresses hepatic gluconeogenesis, thereby directly addressing a key source of fasting hyperglycemia [4]. Our results align strongly with those from the landmark UK Prospective Diabetes Study (UKPDS), which established metformin as a cornerstone of diabetes therapy by demonstrating not only its glycemic efficacy but also its benefit in reducing diabetes-related endpoints and mortality in overweight patients [6]. The swift action of metformin is crucial in the early phase of diabetes management, as it can quickly mitigate "glucose toxicity," thereby potentially preserving beta-cell function and creating a more favorable metabolic environment.

Conversely, while the lifestyle modification group also achieved a clinically meaningful HbA1c reduction, its effect was more modest over this 12-week period. This is understandable, as the mechanisms of lifestyle intervention—improved insulin sensitivity through weight loss and increased muscle glucose uptake—are physiological processes that often require more time to reach their full potential. The profound success of our lifestyle group was, instead, unequivocally demonstrated in the anthropometric data. The weight loss of 5.2 kg in the lifestyle group is a remarkable achievement and mirrors the results of intensive lifestyle interventions in larger trials. For instance, the Look AHEAD (Action for Health in Diabetes) study demonstrated that an intensive lifestyle intervention could produce and sustain significant weight loss, leading to improvements in glycemic control, reduced medication needs, and enhanced cardiovascular risk factors [7]. Our study confirms that even in a shorter timeframe, a structured program of dietary caloric restriction and supervised exercise can initiate substantial weight reduction, laying the groundwork for long-term metabolic health.

When considering these results alongside the existing literature, a nuanced clinical picture emerges. Our findings bridge the outcomes of two pivotal trials: the UKPDS, which cemented the role of pharmacotherapy, and the Diabetes Prevention Program (DPP), which proved lifestyle changes could prevent or delay the onset of diabetes in high-risk individuals [5]. This study demonstrates that in newly diagnosed diabetic patients, both strategies are effective, but with different primary strengths. The choice of initial therapy, therefore, should not be a rigid one but should be guided by the patient's clinical presentation and preferences. For a patient with significantly elevated HbA1c at diagnosis, initiating metformin provides a reliable and potent method to achieve glycemic targets swiftly. For a motivated patient with a primary goal of weight loss and a lower baseline HbA1c, a dedicated trial of intensive lifestyle modification is a valid and highly beneficial first step.
Our study has several limitations that must be acknowledged. The 12-week duration, while sufficient to show significant changes, is too short to assess the long-term sustainability of these effects or the incidence of diabetes-related complications. The open-label design may have introduced performance bias, though the use of objective laboratory

measures like HbA1c mitigates this concern. Furthermore, the sample size, though adequate for this initial comparison, limits the generalizability of the findings and the power for subgroup analyses.

CONCLUSION

In conclusion, this study reinforces that metformin and lifestyle modification are not mutually exclusive but rather synergistic strategies. Metformin acts as a powerful pharmacological tool for rapid glycemic correction, while lifestyle intervention targets the fundamental pathophysiology of the disease through weight management. The most comprehensive and effective strategy for the newly diagnosed Type 2 diabetic patient, as suggested by current guidelines, likely involves the prompt initiation of both approaches in tandem. Future research with longer follow-up and larger cohorts is warranted to observe how these initial divergent benefits translate into long-term glycemic durability, cardiovascular health, and patient quality of life.

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